The over-prescription of opioids for chronic musculoskeletal pain in UK primary care: results from a cohort analysis of the COPERS trial

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ABSTRACT

Objective

To establish the level of opioid prescribing for patients with chronic musculoskeletal pain in a sample of patients from primary care and to estimate prescription costs.

Design

Secondary data analyses from a two-arm pragmatic randomised controlled trial (COPERS) testing the effectiveness of group self-management course and usual care against relaxation and usual care for patients with chronic musculoskeletal pain. (ISRCTN 24426731)

Setting

25 general practices and 2 community musculoskeletal services in the UK (London and Midlands)

Participants

703 chronic pain participants; 81% white, 67% female, enrolled in the COPERS trial.

Main outcome measures

Anonymised prescribing data over 12 months extracted from GP electronic records.

Results

Of the 703 trial participants with chronic musculoskeletal pain, 413 (59%) patients were prescribed opioids. Among those prescribed an opioid, the number of opioid prescriptions varied from 1 to 52 per year. A total of 3,319 opioid prescriptions were issued over the study period, of which 53% (1,768/3,319) were for strong opioids (tramadol, buprenorphine, morphine, oxycodone, fentanyl and tapentadol). The mean number of opioid prescriptions per patient prescribed any opioid was 8.0 (SD=7.9). A third of patients on opioids were prescribed more than one substance; the most frequent combinations were: codeine plus tramadol and codeine plus morphine. The cost of opioid prescriptions per patient per year varied from £3 to £4,844. The average annual prescription cost was £24 (SD=29) for patients prescribed weak opioids and £174 (SD=421) for patients prescribed strong opioids. Approximately 40% of patients received >3 prescriptions of strong opioids per year, with an annual cost of £236 per person.

Conclusions

Long-term prescribing of opioids for chronic musculoskeletal pain is common in primary care. More than a quarter of patients receiving strong opioids may have been over-prescribed according to national guidelines.

Trial registration number: ISRCTN 24426731 COPERS trial

Strengths and limitations of this study

Strengths of this study are:

- This study presents analyses of opioids prescribing data over 12 months extracted from GP electronic records;
- This study estimates the cost of over-prescribing opioids in primary care.

Limitations of this study are:

- This study does not look at longitudinal changes in prescribing opioids to patients with chronic musculoskeletal pain.
- This study does not attempt to relate opioid prescriptions with treatment effectiveness.

Introduction

"Few things a doctor does are more important than relieving pain … pain is soul destroying".[1] These words from Marcia Angell, former editor-in-chief of the New England Medical Journal, succinctly illustrate the therapeutic need for pain relief. However, prescribers have to balance both benefits and harm to patients from pharmacological treatment. Untreated pain can cause both physical and mental distress. One in five people suffer from chronic pain, the most common sources being back pain (24%) or osteoarthritis (35%).[2 3] Findings from the Global Burden of Disease study highlight musculoskeletal conditions as the largest cause of disability in the UK.[4] Pain is the main symptom of many musculoskeletal conditions and it is closely associated with depression, anxiety, fatigue and sleep deprivation. The WHO recognizes chronic musculoskeletal pain as a global priority and aims to better alert nations to the health and economic costs brought about by musculoskeletal conditions.[5]

Opioids are a popular form of analgesia. Up to 90% of individuals presenting to pain centres receive opioids.[6] There is a lack of evidence supporting the efficacy of opioids for chronic non-malignant pain management. Several studies have demonstrated that opioids achieve negligible improvements in pain, function and quality of life.[7-10] In addition, as prescribed doses of opioids increase so does the risk of adverse effects such as depression, anxiety, headaches, insomnia, inadvertent

overdose and death.[11] According to a UK Office of National Statistics report,[12] accidental drug overdose is rising, with the highest number recorded since comparable records began in 1993. Of the 3,346 drug poisoning deaths registered, 53% involved an opiate drug.[12] The UK guidelines on chronic pain management for people with low back pain and osteoarthritis [13-16] recommend weak opioids as a second-line treatment when the first-line medication (NSAIDS, paracetamol or coxibs) is ineffective or not tolerated. Strong opioids are to be only prescribed for unremitting cases and even then for short term use only, stepping patients down to weaker opioids as appropriate, or removing altogether if not effective.[15]

In past years, there has been a range of publications from both media and the medical profession suggesting that prescribed opioid doses are too high and are prescribed for too long, actually endangering patients.[17-19] An editorial in The BMJ entitled: “Opioids in the UK: What is the problem?”[20] concisely summarised concerns from the growing qualitative literature on the over-prescription of opioids for chronic non-malignant pain. There is a growing apprehension that the rise in drug-related deaths parallels a rise in opioid prescriptions.[9 21-23] However, this is an argument based upon evidence from the USA, where rising numbers of deaths have involved prescription drug overdoses.[24-26] There are few reliable data on opioid prescriptions in the UK to infer whether over-prescription is an issue.

In this study our aim was to explore opioid prescribing in a sample of chronic musculoskeletal pain patients in primary care and to estimate the associated costs. We conducted secondary analyses of prescription data from the COPERS trial: a randomised, multi-centre, pragmatic trial of a non-pharmacological group intervention for people with chronic musculoskeletal pain conducted across 27 general practices and musculoskeletal services across the UK.[27-29] We undertook a secondary analysis looking at the entire cohort of patients to characterise patterns of opioid prescription and to estimate the opioid prescription cost. We also looked at the regional differences in opioid prescribing between two UK geographical areas - London and the Midlands.

Methods

Data sources and study characteristics

We used an anonymised database from the COPERS trial that contained the prescription data for the 703 participants. Study design, setting and participants' characteristics are described in detail elsewhere.[28 29] Briefly, COPERS was a multi-centre, pragmatic, randomised controlled effectiveness and cost-effectiveness trial conducted in the UK from 2011 to 2012. Seven hundred and three adults with musculoskeletal pain were randomised using a ratio 1.33:1 to intervention (n=403) or control (n=300). In the intervention group, the participants had usual care and were offered a group self-management intervention using cognitive behavioural

approaches for the non-pharmacological management of chronic pain (the COPERS course). The primary outcome was pain-related disability at 12 months (Chronic Pain Grade disability subscale). There were a wide range of secondary outcome measures which included the Hospital Anxiety and Depression Scale (HADS), health care resource use, and EQ-5D-3L. Health care resource use data included information on the number of contacts with primary and secondary health care services, and prescribing data which were collected from participants' GP electronic records at 12 months. There were no serious adverse events reported in the trial. The study did not find any significant differences in prescribing opioids between the intervention and control groups.[29] We therefore conducted cohort analyses using data for both groups to characterise opioid prescribing for people with chronic musculoskeletal pain.

Participants

The characteristics of study participants and recruitment procedures are described elsewhere.[27] Briefly, participants were adults (≥18 years) with musculoskeletal pain of at least three months duration. Causes of pain included, but were not restricted to: osteoarthritis, back pain, chronic widespread pain, and fibromyalgia. Participants were recruited in the UK (London and the Midlands) from primary care, community musculoskeletal pain services, and secondary care pain services. Exclusion criteria were: inability to give informed consent, not fluent in English, chronic pain arising from active malignant disease or inflammatory arthritis, terminal illness, or serious uncontrolled mental health or substance abuse preventing individuals from participating in the group sessions. The demography of the study participants was: 67% female, mean age 60 years (52 years in London and 67 in Midlands) and 81% white British.

Prescription analysis

We extracted and anonymised prescribing data over 12 months from participants' GP electronic records. The dataset included information on: formulation, dose/strength, and the number of prescription items for each participant. A "prescription" refers to a single medicine prescribed by a doctor on a prescription form. The dataset contained 40,649 prescriptions in total; these included other items as well as opioids. Opioids were identified in the dataset by their generic (non-proprietary) names using the BNF classification system.[30] Searches were conducted for strong opioids: buprenorphine, diamorphine, dipipanone, fentanyl, morphine, oxycodone, papaveretum, pentazocine, pethidine, tapentadol and tramadol, and weak opioids: codeine, dihydrocodeine and meptazinol. We also searched for

combination formulations which contained weak opioids: co-codamol (codeine phosphate/paracetamol) and co-dydramol (dihydrocodeine/paracetamol). The searches were conducted using wildcards and the VLOOKUP option in Microsoft Excel. The two-way multivariate analysis of variance (MANOVA) was conducted using IBM SPSS Statistics. The cost of opioid prescriptions was calculated using the Prescription Cost Analysis (PCA) database[31] using a net ingredient cost per item (cost without discount and dispensing fees per single item prescribed on a prescription form). The list of costs used in the study is shown in Appendix 1. We did not compare oral morphine equivalent doses due to lack of consistency in the conversion ratios taken from different sources.[32-34]

Results

For the 703 study participants, 413 (59%) were prescribed opioids. In total, 3,319 opioid prescriptions were issued over the 12-month period, of which 53% (1,768/3,319) were for strong opioids (tramadol, buprenorphine, morphine, oxycodone, fentanyl and tapentadol). The number of opioid prescriptions varied from 1 to 52 per person per year. The average number of opioid prescriptions per patient was 8.0 (SD=7.9). Table 1 shows the annual numbers of opioid prescriptions and their costs. The cost per prescription varied from £4 to £63 with oxycodone being the most costly opioid prescription. The overall cost of all prescribed opioids during the 12 month study period was £44,491 (on average £63.29 per participant).

Table 1. Annual numbers of prescriptions and their costs (N=413)

Opioid	Number of prescriptions	Cost, £	Average cost per prescription, £
Buprenorphine	391	14,204	36
Codeine/dihydrocodeine	1,551	6,899	4
Fentanyl	41	2,024	49
Morphine	288	3,658	13
Oxycodone	183	11,484	63
Tapentadol	9	356	40
Tramadol	856	5,864	7
TOTAL	**3,319**	**44,491**	30

Figure 1 shows the proportions of prescribed opioids. Oral opioids comprised 87%, transdermal 13%, and parenteral 0.12% of all opioids prescribed. The most frequently prescribed opioid was codeine (47%) which also included combination formulations co-codamol (codeine phosphate/paracetamol) and co-dydramol (dihydrocodeine/paracetamol). Tramadol was the most frequently prescribed strong opioid (26%) followed by buprenorphine (12%), morphine (9%) and oxycodone (6%). Parenteral morphine was prescribed to one patient only, although we do know whether this was for chronic pain or for acute pain management. Figure 2 illustrates the co-prescribing of different opioids in the cohort of patients with chronic

musculoskeletal pain. A combination of opioids was prescribed to 32% (132/413) of patients. Among these 112 (27%) people received two different types of opioids, 17 (4%) three different opioids and 3 people (1%) were prescribed more than three different opioids. The most frequent combination of opioids was codeine plus tramadol (83 people) followed by codeine plus morphine (19 people), codeine plus buprenophine (19 people) and morphine plus tramadol (15 people).

Table 2 summarises numbers of people prescribed different opioids in the entire cohort and in the two samples (London and the Midlands). The proportion of people with musculoskeletal pain prescribed opioids was higher in the Midlands sample (63%) compared to the London sample (56%). Morphine was more frequently prescribed in the Midlands (10%) compared to London (3.7%). The average number of opioid prescriptions per patient was also higher in the Midlands sample 8.58 (SD 8.12) compared to the London sample 7.33 (SD 7.56), although this difference was not statistically significant. The proportions of patients receiving different combinations of opioids were similar in the London and the Midland samples. MANOVA tests conducted using prescription numbers for different opioids showed no significant differences between London and Midlands samples (P>0.05, not shown).

Table 2. Characteristics of opioid prescriptions in the London and Midlands samples.

Prescription characteristics	**London (N=320)**		**Midlands (N=383)**		**Full sample (N=703)**	
	N	**%**	**N**	**%**	**N**	**%**
Prescribed opioids	180	56	233	61	413	59
Buprenorphine	21	6.6	24	6.3	45	6.4
Codeine	130	40.6	150	39.2	280	39.8
Fentanyl	5	1.6	3	0.8	8	1.1
Morphine	9	2.8	35	9.1	44	6.3
Oxycodone	6	1.9	9	2.3	15	2.1
Tapentadol	0	0.0	1	0.3	1	0.1
Tramadol	71	22.2	96	25.1	167	23.8
Single opioid	126	39.4	163	42.6	289	41.1
Combination of opioids	54	16.9	70	18.3	124	17.6
2 opioids	48	15.0	57	14.9	105	14.9
3 opioids	6	3.3	11	4.6	16	2.3
4 opioids	0	0	2	0.8	2	0.5
5 opioids	1	0.6	0	0	1	0.2
Average number of opioid prescriptions over 12 months	7.3 (SD 7.6)		8.6 (SD 8.1)		8.0 (SD=7.9)	

Table 3 summarises prescription characteristics for people receiving weak and strong opioids. More than half of these patients (56%, 231/413) were prescribed strong opioids. Patients taking strong opioids received on average 10 prescriptions

per year with an annual cost of £174 per patient. Among these people 40% received >3 strong opioid prescriptions per year, costing on average £236 per person. Patients taking weak opioids received on average five prescriptions a year with an annual cost of £24 per person. Within this group 21% of people received >3 prescriptions per year costing on average £40 per person.

Table 3. Characteristics of opioid prescriptions in patients receiving strong and weak opioids (N=413)

Prescription characteristics	**People receiving strong opioids N=231**	**People receiving weak opioids N = 182**
Number of patient prescribed opioids	231 (56%)	182 (44%)
Annual number of prescriptions	2,332	987
Annual cost per patient	£174	£24
Average number of prescriptions a year (SD)	10 (9)	5 (5)
Number of patients receiving >3 prescriptions a year	166 (40%)	88 (21%)
Average cost per patient receiving >3 prescriptions a year	£236	£40

Discussion

In this study we characterised opioid prescribing in a sample of people with chronic musculoskeletal pain recruited from primary care into a trial of a self-management intervention. Opioids were prescribed to 59% of study participants and 53% of these prescriptions were for strong opioids, indicating their frequent prescription for patients with chronic musculoskeletal pain. These strong opioids included: tramadol (26%), buprenorphine (12%), morphine (9%) and oxycodone (6%). Approximately 40% of patients received >3 strong opioid prescriptions per year, suggesting long-term prescribing of strong opioids in primary care. According to the national guidelines on chronic pain management for people with low back pain and osteoarthritis,[15 16] strong opioids are to be only prescribed in unremitting cases for short term use, stepping down to weaker opioids, or removing altogether if not effective.[15]

Currently, there is no accepted definition of over-prescribing. The use of this term largely depends on context; it can refer to unnecessary prescription, lack of clinical effectiveness, or side effects.[35-37] In opioid studies over-prescription is closely associated with opioid misuse and abuse.[9 23 38 39] Dunn et al.[9] analysed the relationship between prescribed opioid doses and the risk of overdose in 9,940 patients with chronic non-malignant pain. People receiving daily morphine equivalent doses in the range 50-99 mg have a 3.7-fold increase in overdose risk, while patients receiving doses 100 mg or more had an 8.9-fold increase in overdose risk compared

to patients prescribed <20 mg/day.[9] Given that opioids differ in their potency, formulation and administration routes, converting opioid doses to oral morphine would be one way of identifying the over-prescription of opioids. However, there are differences in the conversion ratios to oral morphine used in the national guidelines and formularies.[32-34] There is also individual variation in patient response to opioids in terms of metabolism, distribution and receptor dynamics.[40 41] Therefore, opioid conversion ratios are purely guidelines that provide starting points for switching between different opioids for the majority of individuals, subject to further assessment and dose titration.

In the context of this study, over-prescribing can be defined as the long-term prescribing of strong opioids (>3 prescriptions a year). This is consistent with NICE guidelines on chronic pain management, which recommend strong opioids to be prescribed for a short time only.[15 16] We found that 40% of patients receiving opioids for chronic musculoskeletal pain may be over-prescribed. The estimated cost of over-prescription was £236 per person per year (Table 3). According to recent analyses of opioid prescribing the UK primary care, 1.25 to 1.38 million people with musculoskeletal conditions receive long-term opioids.[42] Assuming that 40% of these people are over-prescribed, the cost of opioid over-prescription may be over a hundred million pounds a year. This does not include costs associated with the management of side effects and overdose. We were unable to calculate these costs since there were no opioid-related adverse events in our study.[29]

Although our understanding of chronic pain management has advanced, the effective treatment of chronic pain remains elusive. In the chronic pain management guidelines for Australia, Canada, Germany, USA and UK, weak opioids are considered a treatment option.[15 16 43-45] Opioids are used to treat both acute and chronic pain, despite pain experts being in agreement over their poor effectiveness for the latter.[46-48] Some report suggest that prescribing opioids for chronic pain may be associated with poorer functional outcomes compared to other treatment strategies.[49 50] Since the late 1990s, under growing public pressure and aggressive pharmaceutical marketing to eliminate pain, physicians globally have been ever more proactive in their efforts to identify and treat chronic pain. In the UK, the latest published data show that from 2005 to 2015 use of analgesics rose by 21 million items, increasing costs by £230.1 million.[51] Among opioids, the increase was 10% for oxycodone, 9% for morphine and 9% for buprenorphine.[51] Nevertheless, pain intensity does not improve in chronic pain patients on higher opioid doses compared to lower, indicating poor efficiency in current opioid prescription practice.[7-9] Scientific literature is flooded with information on the dangers of opioid misuse, abuse and addiction as a recreational drug.[52-54] However, fatalities from recreational opioid misuse are now overshadowed by medically-prescribed opioid related deaths; in the USA these accounts for 60% of opioid-related deaths[55] and data from the National Center for Health Statistics show that opioid deaths have increased above that of the

deaths from heroin and cocaine combined.[56] Physicians have raised the alarm about the rise in opioid prescribing in primary care, saying that in many cases doses are too high and treatments are too long [17-19] [57] Current guidelines for the management of conditions associated with chronic pain[14-16] reiterate importance of maintaining physical activity, physiotherapy and education programmes. In recent decades, a more holistic approach to chronic pain management has been taken. New treatments involve self-management, coping strategies such as distraction or relaxation techniques, and lower doses of pain relief medication.[58] [59] The purpose of chronic musculoskeletal pain management is to enable the individual to live with the pain, yet limit its impact on their daily functioning, adhering more closely to a biopsychosocial model of health[60]. The cost-effectiveness of these therapies is yet to be established. The study of a non-pharmacological intervention for people with chronic musculoskeletal pain, which generated data for this manuscript, did not find any significant effect on pain severity.[28] [29] However, the intervention was found to be cost-effective due to a reduction in depression and an improvement in health-related quality of life[28] [29]. Researchers recognise the importance of assessing multiple outcomes in pain management studies and that research in pain management should go beyond comparing the clinical effectiveness of different treatments, but address questions of "what treatment is effective, for which patients, on what outcomes, under what circumstances, and at what cost".[61]

Limitations

This study provides a snapshot of opioid prescribing in primary care over a period of one year; it did not look at longitudinal changes in prescribing opioids to patients with chronic musculoskeletal pain.

This study focused on the economic aspects of opioid prescribing; it did not attempt to relate opioid prescriptions with treatment effectiveness.

Our analysis assumes that all opioid prescriptions were for chronic pain and not for acute pain episodes.

Conclusions

Long-term prescribing of opioids for chronic musculoskeletal pain is common in primary care. More than a quarter of patients receiving strong opioids may have been over-prescribed according to national guidelines. The estimated cost of over-prescribing opioids in UK primary care may be around one hundred million pounds a year.

Contributors: TA and NH jointly conducted data analysis, wrote the first draft and integrated comments from the co-authors. DC, SJCT, KH, SE, AS, AR, JF and MRU critically revised the manuscript and provided methodological input. NH led data analyses and manuscript production. MU and SJCT were the principal investigators on the COPERS project. DC, SE, AS and AR were co-applicants on the funding application. All co-authors contributed to the concept of the paper.

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Ethical approval: Cambridgeshire Ethics Committee provided a favourable ethical review for this study Ref: 11/EE/046.

Data sharing: No additional data available.

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Figure 1. Proportional distribution of opioid prescriptions in the overall cohort of patients

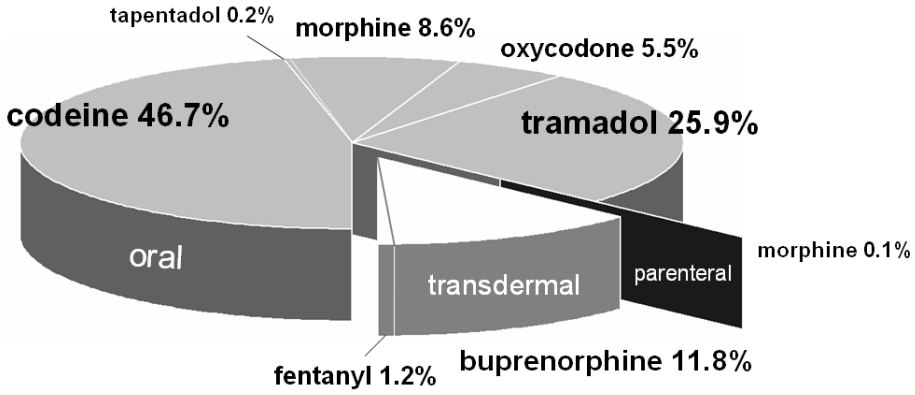
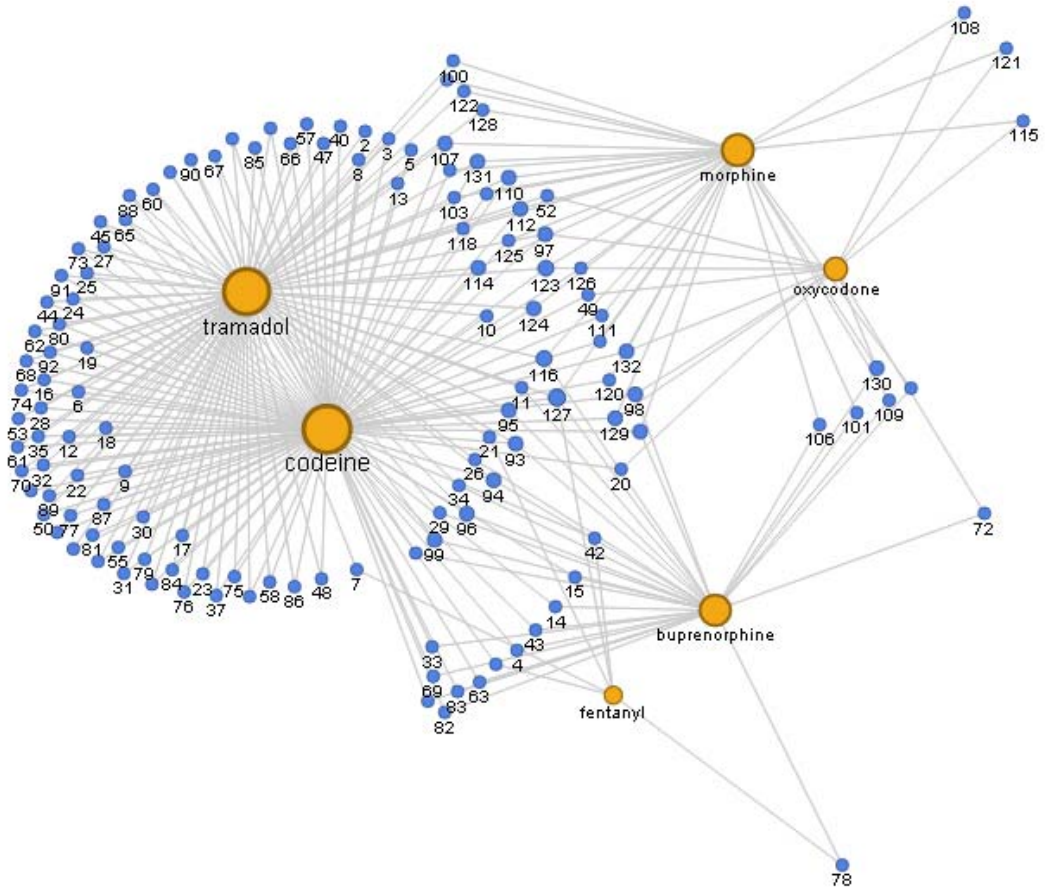


Figure 2. Network plot showing co-prescribing of opioids for 132 patients. Patients are indicated by blue circles with numbers, which are linked to prescribed opioids (yellow circles). The size of the circles is proportional to the number of prescribed opioids.



Appendix 1. Unit costs used for costing opioids prescribed in the study. Costs were taken from the Prescription Cost Analysis database (PCA 2013). PCA data cover all prescriptions dispensed in the community in England (i.e. by community pharmacists, appliance contractors, dispensing doctors, and items personally administered by doctors). PCA costs may differ from the BNF and the NHS Drug Tariff list prices since these costs may be averaged between different pack sizes.

Prescription item including strength	Net ingredient cost per item (£)
Buprenorphine BuTrans_Transdermal Patch 10mcg/hr	32.15
Buprenorphine BuTrans_Transdermal Patch 20mcg/hr	60.65
Buprenorphine BuTrans_Transdermal Patch 5mcg/hr	17.47
Buprenorphine Transdermal Patches 5205 micrograms/hour	23.61
Buprenorphine Transtec_T/Derm Patch 35mcg/hr (20mg)	27.29
Buprenorphine Transtec_T/Derm Patch 5205mcg/hr (30mg)	42.93
Buprenorphine Transtec_T/Derm Patch 70mcg/hr (40mg)	61.99
Co-Codamol (Codeine Phos/Paracetamol) Co-Codamol Eff_Tab 30mg/500mg	9.19
Co-Codamol (Codeine Phos/Paracetamol) Co-Codamol Eff_Tab 8mg/500mg	4.91
Co-Codamol (Codeine Phos/Paracetamol) Co-Codamol_Cap 30mg/500mg	6.06
Co-Codamol (Codeine Phos/Paracetamol) Co-Codamol_Cap 8mg/500mg	5.60
Co-Codamol (Codeine Phos/Paracetamol) Co-Codamol_Tab 15mg/500mg	8.61
Co-Codamol (Codeine Phos/Paracetamol) Co-Codamol_Tab 30mg/500mg	3.77
Co-Codamol (Codeine Phos/Paracetamol) Co-Codamol_Tab 8mg/500mg	3.05
Co-Codamol (Codeine Phos/Paracetamol) Codipar_Cap 15mg/500mg	6.59
Co-Codamol (Codeine Phos/Paracetamol) Kapake_Cap 30mg/500mg	9.29
Co-Codamol (Codeine Phos/Paracetamol) Solpadol_Tab Eff 30mg/500mg	11.37
Co-Codamol (Codeine Phos/Paracetamol) Zapain_Cap 30mg/500mg	4.54
Co-Codamol (Codeine Phos/Paracetamol) Zapain_Capl 30mg/500mg	3.15
Codeine Phosphate Codeine Phos_Linct 15mg/5ml	1.84
Codeine Phosphate Codeine Phos_Liq Spec 10mg/5ml	221.50
Codeine Phosphate Codeine Phos_Tab 15mg	4.41
Codeine Phosphate Codeine Phos_Tab 30mg	3.74
Co-Dydramol (Dihydrocodeine/Paracet) Co-Dydramol_Tab 10mg/500mg	3.18
Dihydrocodeine Tartrate Dhc Continus_Tab 60mg	5.80
Dihydrocodeine Tartrate Dihydrocodeine Tart_Tab 30mg	4.21
Fentanyl Durogesic DTrans_T/Derm Patch 12mcg	24.80
Fentanyl Durogesic DTrans_T/Derm Patch 25mcg	37.68
Fentanyl Durogesic DTrans_T/Derm Patch 50mcg	72.39
Fentanyl Fentalis Reservoir_T/Derm Patch 50mcg/hr	83.04
Fentanyl Fentanyl_Transdermal Patch 100mcg/hr	130.95
Fentanyl Fentanyl_Transdermal Patch 12mcg/hr	22.52
Fentanyl Matrifen_Patch 12mcg/hr	18.34
Morphine 30mg modified release capsules	12.41

Morphine Sulphate Filnarine SR_Tab 10mg	3.79
Morphine Sulphate Morph Sulph_Inj 20mg/1ml Amp	28.33
Morphine Sulphate Morph Sulph_Oral Soln 10mg/5ml	4.97
Morphine Sulphate Morph Sulph_Tab 10mg M/R	6.09
Morphine Sulphate Morphgesic SR_Tab 10mg	4.55
Morphine Sulphate Mst Continus_Susp Gran Sach 100mg	155.70
Morphine Sulphate Mst Continus_Susp Gran Sach 200mg	375.89
Morphine Sulphate Mst Continus_Susp Gran Sach 60mg	91.29
Morphine Sulphate Mst Continus_Tab 10mg	6.09
Morphine Sulphate Mst Continus_Tab 15mg	8.40
Morphine Sulphate Mst Continus_Tab 30mg	11.89
Morphine Sulphate Mst Continus_Tab 5mg	2.88
Morphine Sulphate MXL_Cap 150mg	43.35
Morphine Sulphate MXL_Cap 30mg	12.99
Morphine Sulphate MXL_Cap 60mg	15.49
Morphine Sulphate oral solution 20mg/5ml	18.59
Morphine Sulphate Oramorph_Oral Soln 10mg/5ml	5.00
Morphine Sulphate Sevredol_Tab 10mg	6.62
Morphine Sulphate Sevredol_Tab 20mg	15.19
Morphine Sulphate Zomorph_Cap 10mg	4.07
Morphine Sulphate Zomorph_Cap 30mg	7.65
Oxycodone HCl/Naloxone HCl Targinact_Tab 10mg/5mg M/R	35.42
Oxycodone HCl/Naloxone HCl Targinact_Tab 20mg/10mg M/R	70.12
Oxycodone HCl/Naloxone HCl Targinact_Tab 5mg/205mg M/R	29.18
Oxycodone Hydrochloride Carexil_Tab 10mg M/R	31.75
Oxycodone Hydrochloride Carexil_Tab 5mg M/R	37.00
Oxycodone Hydrochloride OxyContin_Tab 10mg M/R	25.21
Oxycodone Hydrochloride OxyContin_Tab 15mg M/R	30.36
Oxycodone Hydrochloride OxyContin_Tab 20mg M/R	50.58
Oxycodone Hydrochloride OxyContin_Tab 30mg M/R	63.85
Oxycodone Hydrochloride OxyContin_Tab 40mg M/R	96.54
Oxycodone Hydrochloride OxyContin_Tab 5mg M/R	21.59
Oxycodone Hydrochloride OxyContin_Tab 60mg M/R	130.13
Oxycodone Hydrochloride OxyContin_Tab 80mg M/R	219.73
Oxycodone Hydrochloride OxyNorm_Cap 10mg	30.03
Oxycodone Hydrochloride OxyNorm_Cap 5mg	14.12
Oxycodone Hydrochloride OxyNorm_Oral Soln 5mg/5ml S/F	14.43
Tapentadol Hydrochloride Palexia_SR Tab 100mg	48.93
Tapentadol Hydrochloride Palexia_Tab 50mg	27.76
Tramadol Hydrochloride Aceon_Tab 200mg M/R	43.25
Tramadol Hydrochloride Marol_Tab 100mg M/R	8.44
Tramadol Hydrochloride Marol_Tab 150mg M/R	10.53
Tramadol Hydrochloride Marol_Tab 200mg M/R	14.24
Tramadol Hydrochloride Maxitram SR_Cap 100mg	14.41
Tramadol Hydrochloride Maxitram SR_Cap 50mg	5.29

Tramadol Hydrochloride Tradorec XL_Tab 200mg	18.98
Tramadol Hydrochloride Tradorec XL_Tab 300mg	25.45
Tramadol Hydrochloride Tramacet_Tab 3705mg/325mg	16.27
Tramadol Hydrochloride Tramacet_Tab Eff 3705mg/325mg	13.02
Tramadol Hydrochloride Tramadol HCl_Cap 100mg M/R	21.68
Tramadol Hydrochloride Tramadol HCl_Cap 150mg M/R	21.89
Tramadol Hydrochloride Tramadol HCl_Cap 200mg M/R	28.67
Tramadol Hydrochloride Tramadol HCl_Cap 50mg	3.24
Tramadol Hydrochloride Tramadol HCl_Cap 50mg M/R	8.80
Tramadol Hydrochloride Tramadol HCl_Tab 100mg M/R &gn	20.19
Tramadol Hydrochloride Tramquel SR_Cap 150mg	20.60
Tramadol Hydrochloride Tramquel SR_Cap 50mg	8.68
Tramadol Hydrochloride Zydol_Tab Solb 50mg	13.30